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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,909	10/29/2003	James B. Lorens	7946-79836-01	9257

74839 7590 03/18/2010

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EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
03/18/2010	ELECTRONIC

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JAMES B. LORENS, ROBERT E. ATCHISON,
ANNABELLE FRIERA, and SACHA HOLLAND

Appeal 2009-011194[1]
Application 10/696,909
Technology Center 1600

Decided: March 16, 2010

Before RICHARD M. LEBOVITZ, FRANCISCO C. PRATS, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims to methods for identifying compounds that inhibit angiogenesis. The Examiner rejected the claims as anticipated and obvious.

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[1] Rigel Pharmaceuticals, Inc., is the real party in interest (App. Br. 2).

We have jurisdiction under 35 U.S.C. § 6(b). We affirm the anticipation rejection but reverse the obviousness rejection.

STATEMENT OF THE CASE

Claims 1, 12, 14-18, 27, 41-44, and 54-61 are pending and on appeal (App. Br. 2). Claims 1, 27, and 56 are representative of the appealed subject matter and read as follows:

> 1. A method for identifying a compound that inhibits angiogenesis, the method comprising:
>
> assaying *in vitro* kinase activity of an Axl polypeptide comprising an amino acid sequence with greater than about 95% identity to full length SEQ ID NO: 4 in the presence of the compound, wherein the Axl polypeptide has kinase activity in the absence of said compound; and
>
> performing a cell-based assay in an endothelial cell comprising said Axl polypeptide in the presence of the compound, which assay produces an angiogenesis phenotype in said endothelial cell in the absence of the compound,
>
> wherein inhibition of the *in vitro* kinase activity of the Axl polypeptide in the presence of the compound and inhibition of the angiogenesis phenotype in the cell-based assay in the presence of the compound identifies the compound as a compound that inhibits angiogenesis.
>
> 27. An *in vitro* method for identifying a compound that inhibits angiogenesis, the method comprising:
>
> contacting the compound with an endothelial cell that expresses a recombinant Axl polypeptide comprising an amino acid sequence with greater than about 95% identity to full length SEQ ID NO: 4, wherein the Axl polypeptide has kinase activity in the absence of said compound; and
>
> performing a cell-based assay, which assay produces an angiogenesis phenotype in said endothelial cell in the absence of the compound,
>
> wherein inhibition of the angiogenesis phenotype in the cell-based assay in the presence of the compound identifies the compound as a compound that inhibits angiogenesis.

> 56. A method for identifying a compound that inhibits angiogenesis, the method comprising:
>
> contacting the compound with a cell expressing a recombinant Axl polypeptide comprising an amino acid sequence with greater than about 95% identity to full length SEQ ID NO: 4, wherein the Axl polypeptide has kinase activity in the absence of said compound; and
>
> assaying the kinase activity of the Axl polypeptide,
>
> wherein inhibition of the kinase activity of the Axl polypeptide in the presence of the compound identifies the compound as a compound that inhibits angiogenesis.

The Examiner cites the following documents as evidence of unpatentability:

Ruoslahti	US 6,180,084 B1	Jan. 30, 2001
Panzer	US 2004/0048253 A1	Mar. 11, 2004
Klinghoffer	US 2004/0077574 A1	Apr. 22, 2004

Aileen M. Healy et al., *Gas 6 promotes Axl-mediated survival in pulmonary endothelial cells*, 280 AM. J. PHYSIOL. CELL MOL. PHYSIOL. L1273-L1281 (2001).

Judith A. Varner et al., *Integrins and cancer*, 8 CURRENT OPINION IN CELL BIOLOGY 724-730 (1996).

The following rejections are before us for review:[2]

(1) Claims 1, 14, 27, 54-56, and 61, rejected under 35 U.S.C. § 102(b) as being anticipated by Healy (Ans. 3-6); and

(2) Claims 12, 15-18, 41-44, and 57-60, rejected under 35 U.S.C. § 103(a) as being unpatentable over Healy as applied to claims 1, 14, 27, 54-56 and 61, in view of Varner, Ruoslahti, Panzer, and Klinghoffer (Ans. 6-7).

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[2] The Examiner withdrew the appealed rejections under 35 U.S.C. § 112, first and second paragraphs (Ans. 2).

ANTICIPATION

ISSUE

The Examiner finds that Healy discloses "determining the in vitro kinase activity of an Axl polypeptide where the Axl polypeptide has kinase activity in the absence of the compound, see Fig. 5 and page L1276, 2nd col." (Ans. 4).

The Examiner further finds that Healy discloses "performing a cell-based assay in an endothelial cell by contacting human pulmonary endothelial cells that express human Axl (see Fig. 2) with the Axl ligand Gas 6 and determining the effect of this interaction on cell number, see Abstract, p. 1276, left column, and Fig. 6" (*id.*). The Examiner also notes that Healy "teaches assaying apoptosis in human endothelial cells expressing recombinant wild type Axl, see p. L1278 and Figure 9 and 10" (*id.*).

The Examiner further notes that "a wherein clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited, MPEP [§] 2111.04" (*id.*). Therefore, the Examiner reasons, "[g]iven that the method of the prior art comprises the same method steps as claimed in the instant invention, . . . the claimed method is anticipated because the method will inherently be a method for identifying a compound that inhibits angiogenesis" (*id.* at 4-5).

Appellants contend that, although Healy discloses that "contacting human pulmonary artery endothelial cells (HPAEC) which express Axl polypeptide, with exogenous Gas 6 (an Axl ligand) increased Axl phosphorylation . . ., increased cell number . . ., and decreased apoptosis of the cells in serum free medium . . ., these assays are all described independently" (App. Br. 16). Thus, Appellants argue, Healy does not

"teach the *combination* of assaying *in vitro* kinase activity of an Axl polypeptide in the presence of a test compound *and* performing a cell-based assay in the presence of the compound which produces an angiogenesis phenotype in the absence of the test compound, as in claim 1 (*id.* at 15-16).

Moreover, Appellants argue, Healy does not "teach that Gas 6 (an Axl polypeptide agonist) is an angiogenesis inhibitor" (*id.* at 16). Appellants cite the Gallichio[3] reference in support of this assertion (*id.* at 17). Appellants argue that Healy therefore "does not anticipate any of the claims (including independent claims 1, 27, and 56 and any claims that depend from these claims)" (*id.*; *see also* App. Br. 18-19).

Appellants further argue that the independent claims' preambles should be given patentable weight beyond merely reciting an intended purpose of the claimed method "as there has been clear reliance on the preamble to distinguish the claimed invention from Healy *et al.* throughout the prosecution history" (Reply Br. 3).

Appellants also argue that the "wherein" clauses in the independent claims "must be given patentable weight" because, "in order to achieve the claimed invention, one must determine whether the tested compound is an inhibitor of angiogenesis (as opposed to a compound that has no effect on angiogenesis or stimulates angiogenesis)" (*id.* at 4). Thus, Appellants argue,

> [t]his determination is expressed in the wherein clause, such that if the compound inhibits the kinase activity and/or the angiogenesis phenotype in the cell-based assay, then the compound is identified as an inhibitor of angiogenesis (see,

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[3] Margherita Gallichio et al., *Inhibition of vascular endothelial growth factor receptor 2-mediated endothelial cell activation by Axl tyrosine kinase receptor*, 105 BLOOD 1970-76 (2005).

> e.g., specification at page 9, lines 16-22; page 30, lines 6-10). Without the wherein clause, one does not in fact achieve the identification of a compound that inhibits angiogenesis.

(*Id.*).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether Healy discloses a process encompassed by independent claims 1, 27, and 56.

FINDINGS OF FACT ("FF")

1. Healy discloses that "Gas 6, the product of the growth arrest-specific gene 6, is a soluble factor implicated in the regulation of multiple cellular functions, including growth, survival, adhesion, and chemotaxis" (Healy L1273 (citations omitted)).

2. Healy investigated "whether Gas 6 regulates endothelial cell survival at growth arrest. To address this question, we characterized Axl, Rse, and Gas 6 expression in human pulmonary artery endothelial cells (HPAEC)" (*id.* at L1274).

3. Healy "found that the Axl receptor is phosphorylated in untreated cells (Fig. 5, lane 1). Moreover, the addition of exogenous Gas 6 (Fig. 5, lane 2) but not of serum (Fig. 5, lane 3) or protein S (data not shown) enhances Axl phosphorylation 3.5-fold" (*id.* at L1276).

4. Healy discloses that "[o]ur data show that the addition of recombinant human Gas 6 to HPAEC cultures results in a statistically significant increase in cell number (Fig. 6)" (*id.*).

5. Healy discloses "results suggest[ing] that both the endogenous and exogenous Gas 6 function to inhibit HPAEC programmed cell death" (*id.* at L1278).

6. Healy also discloses that, when HPAEC cells expressing exogenous Axl were tested, "Gas 6 decrease[d] the number of apoptotic . . . HPAEC by 54%" (*id.*).

PRINCIPLES OF LAW

"To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997).

During examination, the PTO must interpret terms in a claim using "the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997).

As stated in *In re Zletz*, 893 F.2d 319, 322 (Fed. Cir. 1989), the reason for this rule of interpretation is that "during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed."

Moreover, "[a]bsent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification or prosecution history when those sources expressly disclaim the broader definition." *In re Bigio,* 381 F.3d 1320, 1325 (Fed Cir. 2004). Thus, "while it is true that claims are to be interpreted *in light of* the specification and with a view to ascertaining the invention, it does not follow that limitations from the specification may be read into the claims." *Sjolund v. Musland*, 847 F.2d 1573, 1581 (Fed. Cir. 1988).

Regarding process claims, a preamble recitation that merely expresses the purpose of performing the claimed steps is not a limitation on the process where the body of the claim fully sets forth the steps required to practice the claimed process, and where the preamble recitation does not affect the how the claimed steps are to be performed. *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1375-76 (Fed. Cir. 2001).

Also, "[a] 'whereby' clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim." *Texas Instruments, Inc. v. International Trade Comm.*, 988 F.2d 1165, 1172 (Fed. Cir. 1993).

ANALYSIS

Appellants' arguments do not persuade us that Healy fails to disclose a process encompassed by independent claims 1, 27, and 56.

First, we are not persuaded that those claims' preambles limit the claimed processes to include a positive step of actually identifying a compound that inhibits angiogenesis. For example, the preambles of claims 1 and 56 recite "[a] method *for* identifying a compound that inhibits angiogenesis" (emphasis added). The preamble of claim 27 similarly recites "[a]n *in vitro* method *for* identifying a compound that inhibits angiogenesis" (emphasis added).

Thus, by their terms, the preambles do not require identification of the compound. Rather, the preambles describe the purpose of performing the steps recited in the bodies of the claims. *Cf. Bristol-Myers Squibb v. Ben Venue Labs.*, 246 F.3d at 1375-76 (preamble reciting "method *for* treating cancer patient" (emphasis added) held not to limit claim because recitation "d[id] not result in a manipulative difference in the steps of the claim").

We acknowledge Appellants' argument that the preamble was amended to its current form with the intention of distinguishing over processes that do not identify angiogenesis inhibitors (*see* Reply Br. 3). In the instant case, however, Appellants' argument regarding the scope of the preambles conflicts with the actual language in the preambles. The words of the preambles suggest a purpose for the steps recited in the claims' bodies, rather than another step in an addition to the steps actively recited.

Thus, given the conflict between the preamble interpretation advanced by Appellants and the actual language at issue, we are not persuaded that Appellants' actions during prosecution are sufficient to unambiguously disclaim the plain meaning of the words in the preambles. Rather, as stated in *In re Zletz*, 893 F.2d at 322, "during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed."

Accordingly, given the language in the preambles, and the fact that the claimed steps are performed in the same way whether or not the candidate compound is actually an angiogenesis inhibitor, we are not persuaded that the preambles limit the claimed processes. We therefore do not agree with Appellants that the preambles of claims 1, 27, and 56 should be interpreted as requiring a practitioner performing the claimed processes to actually identify a compound that inhibits angiogenesis.

Nor do we agree with Appellants that the "wherein" clauses in those claims recite a positive step of identifying an angiogenesis inhibitor. For example, claim 1 recites two positive process steps:

> [(a)] assaying *in vitro* kinase activity of an Axl polypeptide comprising an amino acid sequence with greater than about 95% identity to full length SEQ ID NO: 4 in the

> presence of the compound, wherein the Axl polypeptide has kinase activity in the absence of said compound; and
>
> [(b)] performing a cell-based assay in an endothelial cell comprising said Axl polypeptide in the presence of the compound, which assay produces an angiogenesis phenotype in said endothelial cell in the absence of the compound . . . .

Because of the active "assaying" and "performing" language used, it is clear that claim 1 requires a practitioner to perform those steps to be within the scope of the claim.

The wherein clause, however, does not include active language comparable to the active "assaying" and "performing" steps:

> wherein inhibition of the *in vitro* kinase activity of the Axl polypeptide in the presence of the compound and inhibition of the angiogenesis phenotype in the cell-based assay in the presence of the compound identifies the compound as a compound that inhibits angiogenesis.

Rather, given the language used, the wherein clause is reasonably interpreted to identify the conditions that need to be satisfied in order to identify a compound "as a compound that inhibits angiogenesis." Accordingly, while the claim requires that the assays be performed on a compound, there is no step in the claim that additionally requires the compound to have inhibited kinase activity or to have inhibited the angiogenesis phenotype. The "wherein" clause specifies that "inhibition of" the recited activity and phenotype identifies the compound as an inhibitor, but does not recite that a compound achieved a positive result by actually inhibiting the kinase and cell-based activities.

Thus, the wherein clauses at issue are akin to a "whereby" clause that merely states the result of the other features of the claim. As noted above, "[a] 'whereby' clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim." *Texas Instruments v. International Trade Comm.*, 988 F.2d at 1172.

This interpretation squares with Appellants' arguments, which recognize that the wherein clause is conditional in nature: "[t]his determination [of whether a compound is an angiogenesis inhibitor] is expressed in the wherein clause, such that *if* the compound inhibits the kinase activity and/or the angiogenesis phenotype in the cell-based assay, *then* the compound is identified as an inhibitor of angiogenesis" (Reply Br. 4 (emphasis added)).

Thus, while it may be true that the Specification states what an inhibitor is, and also states that the disclosed assays can identify inhibitors (*id.* (citing Spec. 9:16-22 and 30:6-10)), given the conditional nature of the language used in the wherein clauses at issue, we are not persuaded that the wherein clauses require the practitioner to perform either an inhibiting step or an identifying step.

In sum, we agree with the Examiner that the preambles and the wherein clauses of claims 1, 27, and 56 do not require the compound tested in any of the claimed methods to inhibit either the *in vitro* kinase activity of the Axl polypeptide, or the angiogenesis phenotype.

Turning to Healy, we note, as Appellants argue, that the tested compound Gas 6 actually promotes Axl phosphorylation (i.e. kinase) activity rather than inhibits it (FF 3), and also increases cell numbers in culture (FF 4), and decreases apoptosis in cells expressing recombinant Axl (FF 5-6).

As Appellants also argue, it appears that these properties would *not* identify Gas 6 as an angiogenesis inhibitor according to claims 1, 27, and 56.

However, as discussed above, the claims do not require the tested compound to actually inhibit either the kinase or cell-based assays. Thus, the fact that the compound tested in Healy does not inhibit the claim-designated activities does not demonstrate a lack of anticipation.

Lastly, we note that Healy's phosphorylase (i.e. kinase) assay and cell based assays were conducted separately (*see* FF 1-5). However, we do not see, and Appellants do not point to, any recitation in claim 1 regarding the timing of the assays, much less a requirement that the assays be performed simultaneously. Thus, the fact that Healy studied the effects of Gas 6 on Axl expression in different assays performed at different times does not, in our view, demonstrate that Healy does not anticipate claim 1.

In sum, for the reasons discussed, we do not agree with Appellants that the preambles and wherein clauses of independent claims 1, 27, and 56 distinguish those claims from the processes described in Healy. Nor are we persuaded that those claims are otherwise distinguishable over Healy.

We therefore affirm the Examiner's rejection of claims 1, 27, and 56 as anticipated by Healy, as well as claims 14, 54, 55, and 61, which were not argued separately. *See* 37 C.F.R. § 41.37(c)(1)(vii).

OBVIOUSNESS

ISSUE

Claims 12, 15-18, 41-44, and 57-60, rejected under 35 U.S.C. § 103(a) as being unpatentable over Healy as applied to claims 1, 14, 27, 54-56 and 61, in view of Varner, Ruoslahti, Panzer, and Klinghoffer (Ans. 6-7).

The Examiner concedes that Healy does not "teach determining the functional effect by measuring αvβ3 expression or haptotaxis or the use of an antibody, an antisense molecule, an RNAi molecule, or a small organic molecule" (*id.* at 6), and cites Varner, Ruoslahti, Panzer, and Klinghoffer to meet those features (*id.* at 6-7). Based on the references' teachings, the Examiner reasons:

> It would have been *prima facie* obvious at the time the invention was made to perform the method of claim 1 by measuring αvβ3 expression and to use an antibody, antisense molecule, RNAi, or small organic molecule as the compound to use in the screening methods for claims 1, 27, and 56 because the level of αvβ3 expression was known to be important in angiogenesis and the screening of various modulatory compounds for therapeutic purposes was conventionally used in the art at the time of the invention and the advantages of siRNA over other sequence specific modulators was well known in the art at the time the invention was made.

(*Id.* at 7.)

Appellants contend that the Examiner did not "provide any rationale for one of skill in the art to combine or modify the cited references. Taken together, one of skill might be motivated to assay regulation of apoptosis by Axl, but not regulation of angiogenesis" (App. Br. 20). Moreover, Appellants argue "[w]ithout the recognition that inhibition of Axl inhibits angiogenesis, there is no motivation to combine the references and no expectation of success in arriving at Applicants' claimed invention by combining the references" (*id.* at 20-21).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether the evidence of record supports the Examiner's conclusion that an ordinary artisan would have

found claims 12, 15-18, 41-44, and 57-60 prima facie obvious in view of Healy, Varner, Ruoslahti, Panzer, and Klinghoffer.

FINDINGS OF FACT

7. Healy concludes its study by stating:

> Programmed cell death is an integral component of the vascular response to injury. On the one hand, apoptosis in vascular smooth muscle cells counters the exuberant cellular proliferation that leads to intimal thickening. On the other hand, apoptosis in vascular endothelium contributes to pathogenesis by promoting intravascular coagulation activation. *Apoptosis also has a role in the vascular remodeling associated with tumor angiogenesis*. Thus a balance between cell growth and cell death may be required for vascular remodeling. In this report, we characterized the expression and function of the Gas 6 signaling pathway in pulmonary endothelium in vitro. Further elucidation of this pathway will reveal whether Gas 6 functions in maintaining the equilibrium between cell growth and survival in lung endothelium in vivo.

(Healy L1280 (emphasis added).)

8. Varner is a review article that "focus[es] on several of the key recent findings implicating integrin function in tumor proliferation, invasion and angiogenesis" (Varner 724).

9. Varner discloses that "[p]erhaps the most significant of the physiological roles played by integrin αvβ3 in cancer is its critical role in the process of angiogenesis" as evidenced by the fact that it is "minimally, if at all, expressed on resting, or normal, blood vessels, but is significantly upregulated on vascular cells within human tumors and in response to growth factors in vitro and in vivo" (*id.* at 726 (citations omitted)).

10. Panzer discloses "purified human polynucleotides for diagnostics and therapeutics (dithp). Also encompassed are the polypeptides (DITHP) encoded by dithp" (Panzer, abstract).

11. Panzer discloses:

> DITHP encoded by polynucleotides of the present invention may be used to screen for molecules that bind to or are bound by the encoded polypeptides. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit (antagonist), or decrease activity of the polypeptide or the bound molecule. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

(*Id.* at [0735].)

12. Panzer also discloses that the polynucleotides of its invention "are useful in antisense technology" (*id.* at [0754]).

13. Ruoslahti discloses a method for identifying a "molecule that homes to angiogenic vasculature by contacting a substantially purified NGR receptor with one or more molecules and determining specific binding of a molecule to the NGR receptor, where the presence of specific binding identifies the molecule as a tumor homing molecule that homes to angiogenic vasculature" (Ruoslahti, abstract).

14. Ruoslahti discloses that its methods can be used to screen libraries of DNA molecules (*id.* at col. 10, ll. 37-55) as well as antibodies (*id.* at col. 11, ll. 25-37).

15. Klinghoffer discloses "[c] Compositions and methods relating to small interfering RNA (siRNA) polynucleotides are provided as pertains to modulation of biological signal transduction" (Klinghoffer, abstract).

16. Klinghoffer discloses:

> siRNA polynucleotides may offer certain advantages over other polynucleotides known to the art for use in sequence-specific alteration or modulation of gene expression to yield altered levels of an encoded polypeptide product. These advantages include lower effective siRNA polynucleotide concentrations, enhanced siRNA polynucleotide stability, and shorter siRNA polynucleotide oligonucleotide lengths relative to such other polynucleotides (e.g., antisense, ribozyme or triplex polynucleotides).

(*Id.* at [0025].)

PRINCIPLES OF LAW

In *KSR Int' l Co. v. Teleflex Inc.*, 550 U.S. 398, 415 (2007), the Supreme Court emphasized "an expansive and flexible approach" to the obviousness question. The Court also reaffirmed, however, that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* at 418.

Rather, as the Court stated:

> [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements *in the way the claimed new invention does* . . . because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Id. at 418-419 (emphasis added).

Ultimately, therefore, as our reviewing court has stated, "[i]n determining whether obviousness is established by combining the teachings of the prior art, the test is what the combined teachings of the references

would have suggested to those of ordinary skill in the art." *In re GPAC Inc.*, 57 F.3d 1573, 1581 (Fed. Cir. 1995) (internal quotations omitted).

Moreover, "patents are not barred just because it was obvious 'to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.'" *Procter & Gamble Co. v. Teva Pharmaceuticals USA, Inc.*, 566 F.3d 989, 997 (Fed. Cir. 2009) (quoting *In re O'Farrell*, 853 F.2d, 894, 903 (Fed. Cir. 1988)).

ANALYSIS

We agree with Appellants that the Examiner has not made a prima facie case of obviousness with respect to claims 12, 15-18, 41-44, and 57-60.

Claim 12 recites "[t]he method of claim 1, wherein the angiogenesis phenotype is αvβ3 expression, tube formation or haptotaxis." Thus, the "cell-based assay . . . which assay produces an angiogenesis phenotype" must be an assay which detects αvβ3 expression.

We acknowledge Healy's disclosure that apoptosis plays a role in tumor-related angiogenesis (FF 7). We also acknowledge Varner's disclosure that αvβ3 expression plays a significant role in tumor-related angiogenesis (FF 9).

However, Healy's investigation focused on determining the role Gas 6 plays in endothelial cell survival and in Axl-related apoptotic cell death (FF 2, 6). The Examiner has not adequately explained why an ordinary artisan studying the effects of Gas 6 HPAEC on Axl-mediated apoptosis of HPAECs, as taught by Healy, would have been prompted to assay the expression of αvβ3, an angiogenesis marker, in those cells. Moreover, the

Examiner has not pointed to any evidence suggesting that an ordinary artisan would have considered αvβ3 expression relevant, or even useful, in studying Gas 6 or Axl in the manner described in Healy.

The fact that αvβ3 expression *might* have provided *some* useful information regarding Healy's HPAEC cells is, in our view, insufficient to support a conclusion of prima facie obviousness. *See Procter & Gamble v. Teva,* 566 F.3d at 997 ("[P]atents are not barred just because it was obvious 'to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.'")(quoting *In re O'Farrell*, 853 F.2d. at 903).

Accordingly, we reverse the Examiner's obviousness rejection of claim 12.

Claims 15-18 read as follows:

> 15. The method of claim 1, wherein the compound is an antibody.
>
> 16. The method of claim 1, wherein the compound is an antisense molecule.
>
> 17. The method of claim 1, wherein the compound is an RNAi molecule.
>
> 18. The method of claim 1, wherein the compound is a small organic molecule.

Claims 41-44 read essentially identically to claims 15-18, except that they depend from claim 27. Claims 57-60 also read essentially identically to claims 15-18, except that they depend from claim 56.

We acknowledge the suggestions in Panzer, Ruoslahti, and Klinghoffer that antibodies, antisense molecules, interfering RNA

molecules, and small organic molecules are useful as test compounds in inhibition assays (FF 10-16).

However, as noted above, Healy's study focused on specific molecules, Gas 6, Axl, and Rse, and their interactions and effects on HPAECs (FF 1-6). Thus, we are not persuaded that an ordinary artisan performing such studies would have had a reason to substitute antibodies, antisense molecules, interfering RNA molecules, or other small organic molecules, for the Gas 6 molecule studied in Healy's Axl phosphorylase and cell-based assays. Accordingly, we reverse the Examiner's obviousness rejection of claims 15-18, 41-44, and 57-60.

SUMMARY

We affirm the Examiner's rejection of claims 1, 14, 27, 54-56, and 61 under 35 U.S.C. § 102(b) as anticipated by Healy.

However, we reverse the Examiner's rejection of claims 12, 15-18, 41-44, and 57-60 under 35 U.S.C. § 103(a) as being obvious over Healy, Varner, Ruoslahti, Panzer, and Klinghoffer.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

dm

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